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Electrophysiological Assessment of Diabetic Neuropathy Improvements by using Insulin and Thiamine

دراسة الكترو - فسيولوجية للتحسن الوظيفي للأعصاب المحيطية المعتلة باستعمال الأنسولين والثيامين في مرضى داء السكري

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Abstracts

Two groups of (type II) non-insulin dependent diabetes mellitus (NIDDM) patients were assisted electophysiologly for the neuropathy of their peripheral nerves and compared with the control group. The assessments aimed to evaluate the levels of improvements that may occur in the functions of seven peripheral nerves by using insulin (group 1) and thiamine (group 2) as a treatment modalities.

The obtained results of the first visit of the patients of both groups showed significant changes in the recordings of the examined parameters (latency, conductive velocity and amplitude) of the peripheral nerves compared to the recordings of the control group.

The nerves conduction study (NCS) of the newly diagnosed type II diabetic patients who were shifted to insulin gave statistical significant variable improvements at the 12 month of re-examination and in the three parameters of all the tested nerves at the 18 month of re-examination, compared to the first visit of the patients. The effectiveness of thiamine (vit. B1) on the type II diabetic patients seems to be used for the first time, in the present study. The obtained results showed improvement in the tested parameters of three nerves only, namely the median and ulnar sensory nerves in addition to the sural nerves compared to the first visit records of the patients.

Key words: Insulin and Thiamine Effectiveness on Neuropathy of type II diabetic patients.

ملخص

يعتبر اعتلال الأعصاب المحيطية المصاحبة لداء السكري حقلاً خصباً لاهتمام الباحثين والأطباء وخاصة في البحث عن الطرق الناجعة للعلاج وفي هذا الصدد تم دراسة التغيرات في وظائف سبعة أعصاب بالطرق الكهرو-فسيولوجية، وذلك باستدلال سرعة نقل الايعازات العصبية وقياس فترة الكمون الحسي والحركي بالإضافة إلى المدى الكامل للاستجابة العصبية وتم اختيار مجموعتين من مرضى داء السكري غير المعتمد على الأنسولين (Type II) ، المجموعة الأولى حولت الى الأنسولين بينما أعطيت المجموعة الثانية فيتامين ب وتم مقارنة التغيرات الحاصلة في وظائف الأعصاب مع مجموعة ثالثة من الأشخاص الأصحاء ، ولقد تم متابعة التحسن في وظائف الأعصاب لمدة ثمانية عشر شهراً .

لقد برهنت نتائج المجموعة الأولى ان التحسن في الأداء الوظيفي للأعصاب الحركية والحسية كان ذا مدلولاً إحصائياً واضحاً بينما كان التحسن في الأداء الوظيفي للمجموعة الثانية واضحاً في أداء الأعصاب الحسية اكثر منها في أداء الأعصاب الحركية .

The aims of the present study

The prevalence of the two major types of the diabetes mellitus in the populations as reported by (1) are 2% and 0.5% for the type II and type I respectively.

The electrophyiological assessments of the present work aimed to investigate the levels of improvement which may resulted from the insulin and thiamine effectiveness on the type II neuropathic patients.

Introduction

The human nerves system contains about 100 billion neurons. The muscle cells are specilized in contraction function, whereas transmissions of nerve impulses have become the specilized function of neurons (Ganong (2), 1995).

Physiologest showed interest in measuring the speed of conduction of the nerve impulse since long time ago. However the conduction velocity of the nerve impulse was first measured in nerve muscle preparation of the frog (3). The cathode ray oscilloscope was introduced by (4) that improved the recording techniques of nerve impulse measurement. Motor

nerve stimulation with recording of muscle action potentials were introduced by (5), who carried their tests on patients with myasthenia gravis. Recently (2) reported that conduction is an active, self-propagating process that requires expenditure of energy by the nerve. The major part of energy requirement of the nerve is that portion which used to maintain polarization of the membrane. The energy for the nerve is that portion which used to maintain polarization of the membrane. The energy for the Na+ - K+ pump is derived from the hydrolysis of ATP and during the maximal activity, the metabolic rate of the nerve is doubled.

Until the middle of the 19th century the diabetes was considered to be a disorder of the central nervous system. The interest in neurological symptoms that associated with diabetes has continued and in recent years particularly in 1985 the WHO (1) reported that diabetes mellitus is a state of hyperglycemia which may result from many environmental and genetic factors, often acting jointly.

Hyperglycemia may be due to lack of insulin or to an excess of factors that oppose its action. These aspects may lead to abnormalities in the carbohydrate, protein, and lipid metabolism. Its major effects include progressive microvascular disease of retina and kidney, damage to peripheral nerve and excessive arteriosclerosis. The peripheral neuropathy is a clinical syndrome of which the essential features are spontaneous impairment of the function of many peripherals flaccid muscular weakness and sensory abnormalities which affecting the distal more than the proximal segments of the limbs. Sometimes may involve the cranial nerves, with the predominate involvement of the distal lower limbs. They make the most common forms of diabetic neuropathy (6) and as the sensory symptom advances up, the upper limbs become involve (7). These involvement of the lower and upper limbs implicates reductions of endogenous concentration of growth factors particularly of the nerve growth factor (NGF) which shares several molecular, structural and physiologic properties with insulin (8.9). NGF responsive cells respond to the high concentration of insulin in a similar manner (10).

Insulin like growth factors I and II (IGFs) also have been implicated in the pathogenesis of diabetic peripheral neuropathy. IGFs share

structural homology with insulin and insulin itself is an important determinant of the concentration of IGF-I level in the tissues and plays a role in the regulation of IGFs receptors (11). Cultured neurons cannot survive if they exposed to high glucose concentration, this programmed cell death of neurons can be prevented by IGF-I (12).

However because of the diversity of the causative and contributing factors in the pathogenesis of the diabetic neuropathies, no single satisfactory treatment of any of the neuropathic syndromes have been forthcoming (13). Nevertheless there is increasing evidence that the probability of microvascular complications, including neuropathy, is reduced by good glycemic control (14). The study of (15) had strongly suggested that normalization of blood glucose levels have a major effect in preventing microvascular complications including neuropathy.

In addition to insulin, thiamine was also used as a model of treatment for the type II diabetic patients. Thiamine is an organic compound containing pyrimidine and thiazole molecules. Thiamine carries out its function in the body in the form of the coenzyme thiamine pyrophosphate (16). The active form of thiamine is acting in carbohydrate metabolism as coenzyme in the carboxylation of pyruvic and α- ketoglutaric acids and the utilization of pentose in the hexose monophosphate shunt. In thiamine deficiency the oxidation of α- keto acid is impaired and the levels of pyruvic acid in the blood is increased. Thaimine requirements are related to metabolic rate and type of diet and the minimal thiamine requirement in humans are approximates to 0.33 mg/1000 kcal (17). Thiamine deficiency causes sensory-motor neuropathy mostly in the lower extremities. The largest and the longest nerve fibers are the first to be affected and if the deficiency is prolonged, the small nerve fibers degenerate as well (18). The presence of sensorineural deafness has been reported in thiamine dependent megaloblastic anemia in diabetic patients. Reduced (19). pateller tendon reflex was found (20) in thiamine deficiency of the diabetic patients.

Methods and Techniques

For evaluating the level of improvements in the peripheral neuropathy, the type II diabetic patients (age 44 ± 15 years) who were attending Al-Yarmouk Teaching Hospital divided into two groups as shown in Table (1). Insulin was given to each patient of group (1) and thiamine (vit.B1) was given to each patient of group (2) in a does of 50 mg/day. A control group of individuals of comparable ages to the patients and free of impaired glucose tolerance by OGTT were enrolled in the present study. They were of normal weight for height, on usual diet with no drug taken at the time of examination. Renal and liver function test were normal.

Table (1): The groups of diabetic enrolled in the study, indicating the treatment modality.

Group no.	Type of DM	The used drug	Duration of NIDDM	No. of patients
1	Type II	Insulin	Less than one year	25
2	Type II	Thiamine	10 ± 1.7 years	25

Electrophysiological examination of the tested nerves were carried out one time only for the control subjects and four times for the diabetic patients including the first visit and the subsequent re-examinations at the end of 6 , 12 , 18 months. On each visit the ulnar and median nerves of the upper limb, the sural, common peroneal and posterior tibial nerves of the lower limb was tested for latency, conduction velocity and amplitude.

The Neuromatic 2000C apparatus which emploid in the present study, is a fully equipped two channel neuromyograph for clinical EMG, NCS and evoked response. It is a microcomputer controlled instrument, comprising an active electrode box with patient-isolated inputs, EMG-amplifier, averages, monitor loudspeaker, chart recorder, stimulator for NCS and somatosensory evoked responded. The monitor has a wide range of sweep setting and digital display of latency duration.

Action potential from nerves and muscles were evoked by applying pulses from the stimulator, that picked by the electrode tips were fed to the EMG amplifier which is provided by calibration facilities.

Recordings and Measurements

1. Motor nerve conduction recordings (MNCR): The motor latency was measured to the nearest 0.1msec from the onset of the stimulus artifact to the initial of the deflection from the base line of the muscle action potential. The conduction time between the two stimulating points and the difference between the proximal and distal latencies were recorded directly on the screen. The distance between the center of the stimulating cathodes, as measured on the skin following the course of the nerve was taken to be the nerve conduction distance. The motor conduction velocity (MCV) was calculated by dividing the conduction distance (in meters) by the conduction time (in seconds).
2. Sensory nerve conduction recordings (SNCR): The sensory latency was measured from the onset of the stimulus artifact to the intial positive peak of the sensory action potentail (SAP). The nerve conduction distance was measured on the skin between the center of the stimulating cathode and the center of the proximal recording electrode. The sensory conduction velocity (SCV) was calculated directly by dividing the nerve conduction distance (in meters) by the latency value (in second). The amplitude of the nerve action potential was measured from peak to peak (positive to negative deflection from the baseline). The skin was carefully prepared at both the stimulating and the recording sites. It was disinfected by 70% alcohol and gently rubbed to decrease its resistance to the applied current. Maximum response was usually obtained by a current ranged 40-60 and 15-25 mAmp when testing motor and sensory fibers respectively. All the nerves recordings were carried out on the limbs of the right side of the patients. During examination of the median and ulnar nerves the subject lies supine with the arms extended 180^o at the elbow. The knee bent 120^o when the peroneal and posterior tibial nerves were examined.When examined sural nerve, the subject lies prone with a support under the ankle with the knee at an angle of 140^o (21).

	Nerve	Control				1st visit				6 Months				12 Months				18 Months			
		Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs
1	Sural Nerve	2.93 ±0.42	43.65 ±5.4	6.57 ±2.4	91.16 ±15.5	4.09 ±0.99	35.8 ±5.28	4.3 ±1.22	281 ±163.5	3.87 ±0.85	36.2 ±4.14	4.36 ±0.87	163 ±29	3.46 ±0.96	37.4 ±2.8	4.56 ±0.78	124 ±25	3.02 ±0.48	38.8 ±3.15	5.1 ±0.8	108 ±15
						*	*	*	**	N	N	N	**	N	*	*	*	*	*	*	*
2	Comm. Peroneal	3.59 ±0.46	46.02 ±4.2	5.11 ±1.8		4.5 ±1.01	38.45 ±4.47	4.0 ±1.09		4.22 ±0.88	39.6 ±2.44	4.05 ±0.57		3.78 ±0.71	40.3 ±2.21	4.5 ±0.78		3.5 ±0.51	41.5 ±241	4.97 ±0.79	
						N	*	N		N	N	N		*	*	*		*	**	*	
3	Posterior Tibial	3.63 ±0.6	44.12 ±5.2	4.73 ±1.85		4.28 ±0.86	36.4 ±4.7	4.15 ±1.15		4.02 ±0.73	36.7 ±3.81	4.31 ±0.79		3.77 ±0.57	38.9 ±3.05	4.63 ±0.66		3.27 ±0.54	38.2 ±2.3	5 ±0.6	
						N	*	N		N	N	*		*	*	*		*	**	**	
4	Median Sensory	2.74 ±0.4	47.7 ±4.7	8.01 ±2.3		3.60 ±0.67	38.87 ±4.72	5.16 ±1.44		3.34 ±0.6	39.4 ±4.7	5.5 ±1.2		3.15 ±0.46	40.4 ±3.6	5.9 ±1.09		2.7 ±0.32	41.7 ±3.36	6.4 ±0.97	
						*	*	*		N	N	N		N	*	*		*	*	*	
5	Median Motor	3.18 ±0.4	50.2 ±[illegible]	5.7 ±2.0		3.91 ±0.73	38.0 ±5.78	4.2 ±1.43		3.74 ±0.61	39.13± 4.65	4.25 ±1.2		3.25 ±0.36	40.2 ±2.9	4.91 ±0.91		3.20 ±0.29	40.8 ±3.12	5.0 ±0.48	
						N	**	*		N	N	N		*	*	*		*	**	*	
6	Ulnar Sensory	2.34 ±0.4	47.9 ±6.0	7.9 ±2.2		3.58 ±0.72	38.5 ±5.4	5 ±1.4		3.32 ±0.54	39.2 ±4.2	5.17 ±1.19		3.25 ±0.45	40.3 ±3.5	5.45 ±0.97		2.9 ±0.35	41 ±3.1	5.8 ±0.8	
						N	**	**		N	*	*		N	*	*		*	*	**	
7	Ulnar Motor	2.58 ±0.52	50.71 ±5.7	6.2 ±1.8		3.42 ±0.61	38.6 ±4.94	4.1 ±1.3		3.34 ±0.5	40. ±4.5	4.25 ±1.16		3.0 ±0.3	40.5 ±3.39	4.75 ±0.97		2.47 ±0.2	41.2 ±2.5	4.8 ±09	
						N	**	*		N	*	N		N	*	*		*	*	*	

N = Not significant $^{*}p < 0.05$
$^{**}p < 0.005$ $^{***}p < 0.0005$

Table (2): NCS of newly diagnosed type II diabetic patients shifted to insulin

	Nerve	Control				1st visit				6 Months				12 Months				18 Months			
	Nerve	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs	Lat	Vel	Amp	Fbs
1	Sural Nerve	2.93 ±0.42	43.65 ±5.4	6.57 ±2.4	91.16 ±15.5	4.45 ±1.05	39.8 ±6.9	5.64 ±2.05	237 ±59	4.21 ±0.66	39.8 ±5.4	5.7 ±1.27	178 ±44	4.0 ±0.57	41.9 ±2.8	5.7 ±0.93	154 ±26	3.5 ±0.46	42.7 ±2.2	6.36 ±0.8	134 ±18
						*	N	N	**	N	N	N	**	N	*	N	**	*	*	N	**
2	Common Peroneal	3.59 ±0.46	46.02 ±4.2	5.11 ±1.8		5.25 ±1.42	43.96 ±4.47	3.75 ±1.8		5.16 ±0.98	44.0 ±6.53	4.19 ±1.32		5.0 ±0.67	44.7 ±5.1	4.3 ±1.04		4.7 ±0.52	45.7 ±3.29	4.36 ±0.7	
						*	N	N		N	N	N		N	N	N		N	N	N	
3	Posterior Tibial	3.63 ±0.6	44.12 ±5.2	4.73 ±1.85		5.25 ±1.26	42.2 ±5.78	4.27 ±1.9		5.0 ±0.9	43 ±3.7	4.37 ±1.16		4.8 ±0.58	44 ±2.5	4.5 ±0.85		4.59 ±0.43	44.7 ±2.1	5.0 ±0.6	
						*	*	N		N	N	N		N	N	N		N	N	N	
4	Median Sensory	2.74 ±0.4	47.7 ±4.7	8.01 ±2.3		3.85 ±0.91	41.5 ±10.1	6.72 ±1.96		3.5 ±0.69	44.13 ±6.9	6.9 ±1.89		3.26 ±0.59	45.7 ±4.47	7.2 ±1.8		2.88 ±0.56	46 ±3.1	7.65 ±1.85	
						*	*	N		N	N	N		N	*	N		N	*	*	
5	Median Motor	3.18 ±0.4	50.2 ±5.0	5.7 ±2.0		4.05 ±1.02	50.2 ±8.4	5.27 ±2.2		4.04 ±0.82	50.6 ±4.31	5.3 ±1.32		4.0 ±0.66	51 ±3.29	5.4 ±1.07		3.6 ±0.53	51.2 ±3.0	5.84 ±0.9	
						*	N	N		N	N	N		N	N	N		N	N	N	
6	Ulnar Sensory	2.34 ±0.4	4.79 ±6.0	7.9 ±2.2		3.77 ±0.99	43.5 ±7.5	5.23 ±2.4		3.58 ±0.52	44.8 ±4.3	5.62 ±1.59		3.15 ±0.48	45.5 ±3.5	5.75 ±1.52		2.8 ±0.43	46.3 ±3.3	6.04 ±1.4	
						*	*	*		N	N	N		N	*	N		*	*	*	
7	Ulnar Motor	2.58 ±0.52	50.7 ±5.7	6.2 ±1.8		3.87 ±0.55	44.2 ±8.9	5.2 ±1.3		3.8 ±0.48	45.4 ±6.12	5.3 ±0.94		3.75 ±0.4	45.7 ±4.2	5.45 ±0.86		3.29 ±0.3	45.9 ±3.3	5.75 ±0.7	
						*	*	*		N	N	N		N	N	N		N	N	N	

N = Not significant   ** $p < 0.05$*

Table (3): NCS of type II diabetic patients with – 10 years duration, on Thiamine

All the recordings were performed in an air- conditioned room with temperature of 23 ± 2 C^o and the skin temperature of the examined subjects were 34 ± 1.5 C^o, and 35 ± 1.4 C^o for the lower limbs and the upper limbs respectively.

Statistics

Statistical analysis of the obtained recordings were carried out by feeding the data into IBM computer. The arithmetic mean, standard deviation (SD) and correlation coefficient (γ) were calculated by using statistical methods (22). Student's paired and unpaired t- test was used to analyze the differences between the results and if the P- value is greater than 0.05 the result regarded to be insignificant.

Results

1. The tested latency, velocity and amplitude are always mentioned in this order, without their units.
2. The unit for latency is millisecond, for velocity is meter per second and for amplitude is millivolt.
3. The values are expressed as the mean ± SD in the tables but in the paragraphs values are expressed by their means only.
4. The obtained results of the three parameters of the patients first visit is compared to the control group results.

The obtained results of the 6, 12 and 18 visits of the patients are compared to their first visits.

I. Newly dignosed type II diabetic patients given insulin (Table 2)

a. Sural nerve

The recordings of this nerve at the first visit gave significant changes for the three parameters and also for the FBS when compared to the control group results. The FBS levels at the twelve and eighteen months gave significant changes from the first visit level. The

recordings of the parameters at the twelve months showed significant changes only for velocity and amplitude, while the recordings of the eighteen months gave significant changes for the three parameters when compared to the first visit records.

b. *Common Peroneal nerve*

The recording of this nerve at the first visit when compared to the control group records showed significant changes only for velocity. The recordings of the six months later showed no significant changes while the twelve and eighteen months later recordings gave significant changes for the three parameters when compared to the first visit recordings.

c. *Posterior Tibial nerve*

The recordings of this nerve at the first visit gave significant changes only for the velocity when compared to the control group recordings. The recordings of the six months later, showed significant changes only for amplitude, while the twelve and eighteen months recordings showed significant changes in the three parameters when compared to the first visit recordings.

d. *Median nerve- Sensory*

The recordings of this nerve at the first visit when compared to the control group records gave significant changes for the three parameters. Six months later the results gave significant changes for the three parameters compared to the previous visit. The recordings of the twelve month showed significant changes only for velocity and amplitude while that of the eighteen month recordings showed significant changes for the three parameters when compared to the first visit recordings.

e. *Median nerve - Motor*

The recordings of this nerve at the first visit when compared to the control group recordings showed significant changes for the velocity and amplitude. Six months later, the records gave insignificant

changes for the three parameters compared to the previous visit. The twelve and the eighteen months recordings gave significant changes for latency, velocity and amplitude compared to the first visit records.

f. Ulnanr nerve - Sensory

The recordings of this nerve at the first visit when compared to the control group records showed significant changes for velocity and amplitude. The recordings at six and twelve months later showed significant changes only for velocity and amplitude, while the eighteen month records gave significant changes for the three parameters when compared to the first visit.

g. Ulnar nerve- Motor

The recordings of this nerve at the first visit gave significant changes for velocity and amplitude compared to the control group records. Six months later, the recordings showed significant changes only for velocity and twelve months later, the recordings gave significant changes for velocity and amplitude, but the eighteen months later recordings showed significant changes for latency, velocity and amplitude when compared to the first visit records.

II Type II diabetic patients with about 10 years duration given thiamine (Table 3)

a. Sural nerve

The recordings of this nerve in the first visit gave significant changes only for latency when compared to the control group. The FBS level was 237 with $P < 0.005$ compared to the controls. Also the FBS levels showed significant decrease at six, twelve and eighteen months examinations. The re-examinations of the three parameters at the, twelve and eighteen months showed no significant changes for amplitude but gave significant changes in latency and velocity when compared to the first visit recordings.

b. *Common Peroneal nerve*

The recordings of this nerve in the first visit showed significant change only for the latency when compared to the control group recordings. The recordings of six, twelve and eighteen months showed no significant changes for the three parameters, when compared to the first visit recordings.

c. *Posterior Tibial nerve*

The recordings of this nerve, at the first visit, for the three parameters showed significant changes only for latency and velocity when compared to the control recordings. The recordings of the three parameters at six, twelve and eighteen months showed no significant changes when compared to the first visit records.

d. *Median nerve – Sensory*

The recordings of this nerve in the first visit when compared to the control group records showed significant changes for latency and velocity. The recordings at six, twelve and eighteen months respectively gave no significant changes, significant changes only for velocity and significant changes for velocity and amplitude when compared to the first visit recordings.

e. *Median nerve-Motor*

The recordings of this nerve in the first visit gave significant changes only for latency when compared to the control group records. The recordings of six, twelve, and eighteen months showed no significant differences for the three parameters when compared to the first visit recordings.

f. *Ulner nerve- Sensory*

The recordings of this nerve in the first visit gave significant changes for the three parameters when compared to the control group recordings. The re-examination records taken at six, twelve and eighteen months respectively gave no significant changes, significant

difference only for velocity and significant changes for the three parameters when compared to the first visit recordings.

g. *Ulner nerve- Motor*

The recordings of this nerve in the first visit gave significant changes for the three parameters when compared with the control recordings. The re-examined three parameters gave no significant differences at the six, twelve and eighteen months records when compared to the first visit recordings

Discussion and Conclusion

In the present study, almost all patients had shown electrophysiological changes at their first visits compared to the control group, although most patients had no complaints indicating that they may had subclinical neuropathy which ensuring the importance of the nerves conduction study (NCS) in the dignosis of subclinical neuropathy particularly in sustained hyperglycemia. These results are in accordance with the findings of (23, 24, 25).

The presence of subclinical neuropathy in diabetic patients ensured the great harmful effects of hyperglycemia on nerves function as the obtained results indicate that even the short duration of hyperglycemia in the patients of less than one year of type II resulted in a significant changes in all the seven tested nerves when compared to the control group recordings.

Almost similar results were reported by (26). With better glycemic control, by using insulin, all the tested nerves showed variable degrees of significant improvements in the three examined parameters (latency, velocity, amplitude) particularly after 18 months from the first visit of the patients. These results (Table 2) are ensuring the role of better glycemic control on the nerve function. Similar conclusion was reported by (15) that strict glycemic control reduces the risk of clinical neuropathy in patients with diabetes of 1-15 years duration.

The recorded improvements in the electrophysiological parameters of the newely dignosed patients who were shifted to insulin in order to maintain strict glycemic control may indicates the great important of the improvements in carbohydrate metabolism which is obviously having positive influence on nerves function. These results are in good agreement with the recent study by (27) who stated that metabolic control provided by self regulated source of insulin not only halts but also ameliorates nerves function even if polyneuropathy is advanced. Also the present study support the findings which reported by (28, 29, 30) that they confirmed the association of increased levels of diabetic neuropathy with poor glycemic control.

Thiamine (vit. B1) used in the present study to investigate its effectiveness on the peripheral nerves of type II diabetic patients. As far as the literatures concerned, it seems that this is the first time that thiamine is used as a treatment modality of the neuropathic type II patients. The obtained results (Table 3) show that after 18 months of follow up testing seven nerves, only three of them gave significant improvements for the recordings of the parameters. In addition the obtained recordings of the parameters does not show full improvements to reach that records of the control group. These results again emphasize the important role of insulin in improving the peripheral nerves function which could be attributed to the role of insulin in regulating and stabilizing the cell membrane activities and as a sequence improving the neuronal cell functions.

This conclusion is in accordance with the recent publications of (15, 27) who reported that insulin had a direct effects on nerve cell functions in addition to its glycemic control. Also the obtained results indicate that the improvement ability of thiamine, is that out of the seven tested nerves, are only significant in the two sensory nerves, (but not the motor of the upper limbs) and the sural nerve. This result is in accordance with the findings of (6,7,18,31) who reported that the predomenent involvement of the distal lower limbs make the most sensory symptoms advances up. The uper limbs then become involved, the largest and the longest nerve fibers are the first to be affected (32).

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